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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/710,058	11/10/2000	David Anderson	A-68531-1/RMS/JJD/SPL	4112

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EXAMINER	
PONNALURI, PADMASHRI	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 01/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/710,058	**Applicant(s)** ANDERSON ET AL.	
	Examiner Padmashri Ponnaluri	**Art Unit** 1639	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 05 December 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *none*.
   Claim(s) objected to: *none*.
   Claim(s) rejected: *1-3 and 20*.
   Claim(s) withdrawn from consideration: *none*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see the attached.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

PADMASHRI PONNALURI
PRIMARY EXAMINER

Padmashri Ponnaluri
Primary Examiner
Art Unit: 1639

ADVISORY ACTION (continued)

The proposed amendment filed on 12/5/05 has been considered.

The amendment and the response filed on 12/5/05 would not place this application in condition for allowance, and the reasons have been discussed below.

The rejection of Claims 1- 3 and 20 under 35 U.S.C. 103(a) as being unpatentable over Bryan et al. US Pat. No. 6,232,107 (5/01: filed 10/98 or earlier) with attached Result 4 DATABASE Alignment search and Aran et al. Cancer Gene Therapy, Vol. 5, No. 4 pages 195-206 (1998) is maintained for the reasons of record.

The rejection of Claim 20 under 35 U.S.C. 103(a) as being unpatentable over the obviousness rejections using Aran et al. And Bryan et al. as applied to claims 1-3 and 20 above, and, if necessary, further in view of Zolutukhin et al. US Pat. No. 5,874,304 (2/99: filed 1/96) is maintained for the reasons of record.

The rejection of Claims 1-3 and 20 under 35 U.S.C. 103(a) as being unpatentable over Zolutukhin et al. US Pat. No. 5,874,304 (2/99: filed 1/96) and Bryan et al. US Pat. No. 6,232,107 (5/01: filed 10/98 or earlier)with attached Result 4 DATABASE Alignment search, is maintained for the reasons of record.

Applicant's arguments filed on 12/5/05 have been fully considered but they are not persuasive.

The instant claims are drawn to 'a retroviral vector comprising a polynucleotide encoding a green fluorescent protein (GFP) having the amino acid sequence of SEQ ID NO: 2.'

Applicants assert that the claimed vector is retroviral vector and the amino acid sequence of SEQ ID NO: 2 is of the wild type Renilla GFP.

Applicants argue that the results achieved with the claimed invention were unexpected because Applicants found success in an area which others found only failure, namely expression of wild type green fluorescent proteins using a retroviral vector. Applicants further assert that the 'Applicants success was surprising because art at the time the filing shows that wild-type GFPs other than wild type Renilla GFP (i.e., wild type versions of the particular mutant GFP used by Aran, Zolutukhin and others) could not be expressed in a mammalian cells using retroviral vector.

*Applicants arguments and assertions have been fully considered and are not persuasive. The instant claims are drawn to 'retroviral vector comprising a polynucleotide encoding a GFP having the amino acid sequence of SEQ ID NO: 2.' Since the amino acid sequence of SEQ ID NO: 2 is of the wild type Renilla GFP, the claim is interpreted as the 'retroviral vector comprising nucleotide sequence encoding wild type Renilla GFP.' Applicants seem to be arguing that the nucleic acid sequence (wild type nucleic acid sequence of GFP) that encodes the wild type Renilla GFP is not altered (i.e., **wild type**). However, the instant claim 20 contradicts this interpretation by reciting that the polynucleotide comprises a human codon-optimized nucleic acid sequence encoding the Renilla GFP. Thus, the nucleic acid of Renilla GFP is altered (codon optimized) such that the sequence encodes amino acid sequence of wild type Renilla GFP.*

Applicants further refer to several publications Aran, Hanzano, Levy, Cheng and others, who unsuccessfully tried to express wild type Acquoria GFP using retroviral vector. Applicants refer to Aran et al (Cancer Gene Therapy, vol. 5, No.4, 1998, pages 195-206) in support of

applicants position. These publications have been considered and are not persuasive, since the references are specifically drawn to retroviral vectors encoding a wild type Aequorea GFP.

Regarding applicant's reference to the disclosure of Aran reference in page 204, is not persuasive. Applicants interpretation of Aran reference is misplaced. Aran discloses that '...previously synthesized a retroviral vector identical with the ***MDR-IRES-GFP vector by using the wild-type GFP*** *but was unable to detect any fluorescence.... **WtGFP has been show to display much less green fluorescent than the optimized, humanized, red-shifted GFP**, and therefore the level of wtGFP expression obtained from the MDR-IRES-wtGFP vector was not enough to produce a detectable signal.'*

Aran reference is interpreted as teaching that the retroviral vector identical to MDR-IRES-GFP using the wtGFP (unlatered DNA sequence) has displayed much less green fluorescence than the ***optimized, humanized, red-shifted GFP.*** *Thus, the reference clearly teaches retroviral vector comprising codon optimized Aequorea GFP has high level of expression of GFP as compared to the retroviral vector comprising wild type GFP (unlatered DNA). And further Aran teaches retroviral vector with wild type GFP (MDR-IRES-wtGFP) with low levels of wtGFP expression. Thus, Aran was able to express wtGFP in retroviral vector.*

Cheng et al teach the mutated GFPs and retroviral vectors contianing the improved GFP gene. Cheng et al also teaches that the wtGFP expression in cultured mammalian cells emits a detectable green fluorescent signal, at a relatively low level. Thus, Cheng et al clearly teaches retroviral vector expressing wtGFP, and as compared to the mutated GFP, the wtGFP has low level of expression of green fluorescent signal.

Levy et al teach retroviral vectors comprising humanized, codon optimized GFP. Levy et al teach 'comparisions between the wild type GFP, and humanized, serine-65-red shifted mutant GFP demonstrated substantial improvement in fluorescence expression after transfection or retroviral mediated GFP gene transfer.' Thus, the reference clearly teaches that the level of expression of wild-type GFP is low compared to the mutated GFP.

Thus, for the reasons discussed above the references are not considered as supporting applicant's arguments regarding the status of the art the time of filing of the instant application.

And further it has been noted, applicants arguments are directed to the level of expression of green fluorescence signal, however the instant claims are not drawn to the level of expression of the wild type GFP.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., 'low level of expression of wild-type) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants assertions that the results of expressing wild type Renilla GFP in mammalian cells using retroviral vectors is unexpected in view of the prior art is not persuasive. Since the references discussed above provide ample motivation towards 'codon optimization of GFP sequences', and the use of retroviral vectors; and further the references of record teach further advantages of use of Renilla GFP as compared to the Aequorea GFP. Thus for the reasons of record, the obviousness rejections of record have been maintained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

12 January 2006